



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA-1975-N-0355 (formerly 75N-0185), FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), FDA-1978-N-0701 (formerly 78N-0070), FDA-1979-N-0224 (formerly 79N-0169), and FDA-1983-N-0297 (formerly 83N-0030); DESI 1626, 3265, 12283, and 50213]

Drugs for Human Use; Drug Efficacy Study Implementation; Certain Prescription Drugs Offered for Various Indications; Final Resolution of Hearing Requests Under Dockets

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that all outstanding hearing requests pertaining to Docket Nos. FDA-1975-N-0355 (formerly 75N-0185) (DESI 3265); FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), and FDA-1978-N-0701 (formerly 78N-0070) (DESI 1626); FDA-1979-N-0224 (formerly 79N-0169) (DESI 12283); and FDA-1983-N-0297 (formerly 83N-0030) (DESI 50213) have been withdrawn. Shipment in interstate commerce of any of the products identified in these dockets, or any identical, related, or similar (IRS) product to the products in these dockets, that is not the subject of an approved new drug application (NDA) or abbreviated new drug application (ANDA) (other than an over-the-counter (OTC) product that complies with an applicable OTC monograph) is unlawful as of the effective date of this notice.

DATES: Effective Date: This notice is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: All communications in response to this notice should be identified with the appropriate docket number and directed to Sakineh Walther, Division of Prescription Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 5242, Silver Spring, MD 20993-0002, sakineh.walther@fda.hhs.gov.

FOR FURTHER INFORMATION CONTACT: Sakineh Walther, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 5242, Silver Spring, MD 20993-0002, 301-796-3349, sakineh.walther@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

In a notice published in the Federal Register of July 24, 2012 (77 FR 43337) (the July 24, 2012, notice), FDA described the outstanding hearing requests pertaining to, among others, Docket Nos. FDA-1975-N-0355 (formerly 75N-0185) (DESI 3265); FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), and FDA-1978-N-0701 (formerly 78N-0070) (DESI 1626); FDA-1979-N-0224 (formerly 79N-0169) (DESI 12283); and FDA-1983-N-0297 (formerly 83N-0030) (DESI 50213) established under the Agency's Drug Efficacy Study Implementation (DESI) program. In the July 24, 2012, notice, FDA offered an opportunity for companies with outstanding hearing requests under those dockets to withdraw or affirm their outstanding hearing requests.

A. Docket No. FDA-1975-N-0355 (Formerly 75N-0185) (DESI 3265)

In 1971, FDA published DESI efficacy findings for single-ingredient anticholinergic drugs for oral or injectable use containing dicyclomine hydrochloride (HCl), among other ingredients (36 FR 11754, June 18, 1971). In a notice published on November 11, 1975 (40 FR

52644), FDA determined that the June 18, 1971, Federal Register notice should not have included drugs containing certain specified ingredients, including dicyclomine HCl, because the drugs containing those ingredients were not anticholinergic drugs (40 FR 52644 at 52648). Elsewhere in the Federal Register of November 11, 1975 (40 FR 52649), FDA published a notice concluding that dicyclomine HCl products, among other products covered by the notice, were less than effective and offering an opportunity for hearing regarding these drugs.

On June 22, 1984, in response to the submission of data, FDA published a followup notice regarding single entity dicyclomine HCl products (49 FR 25681). In that notice, FDA concluded that such products were effective for the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, and mucous colitis) and established conditions for their marketing and labeling (49 FR 25681 at 25683 and 25684). The Agency also found, however, that the products were lacking substantial evidence of effectiveness for use in the treatment of acute enterocolitis or infant colic (49 FR 25681 at 25684) and offered an opportunity for hearing.

At the time of the July 24, 2012, notice, there was one outstanding hearing request under this docket filed by Merrell-National Laboratories, 110 Amity Rd., Cincinnati, OH 45215, regarding Bentyl Capsules (NDA 7-409), Bentyl Injection (NDA 8-370), Bentyl Syrup (NDA 7-961), and Dactil Tablets (NDA 8-907). FDA believes Sanofi-Aventis U.S. to be the successor-in-interest to Merrell-National Laboratories, but received no response to its attempt to contact Sanofi-Aventis U.S. regarding this hearing request in September 2011. In the July 24, 2012, notice, FDA provided the company an opportunity to affirm or withdraw its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

B. Docket Nos. FDA-1976-N-0272 (Formerly 76N-0056), FDA-1976-N-0344 (Formerly 76N-0057), and FDA-1978-N-0701 (Formerly 78N-0070) (DESI 1626)

In 1972, FDA classified certain combination drug products containing a xanthine derivative as lacking substantial evidence of effectiveness for some labeled indications and possibly effective for other labeled indications (37 FR 14895, July 26, 1972). As described in a Federal Register notice of February 29, 1984 (49 FR 7454), FDA subsequently handled these products in three groups:

Group 1: Combinations containing 2 grains or less of a xanthine derivative, ephedrine, and 8 milligrams (mg) or less of phenobarbital (Docket No. FDA-1976-N-0344 (formerly 76N-0057));

Group 2: Combinations containing more than 2 grains of xanthine derivative, more than 8 mg of phenobarbital, and/or an ingredient not considered as part of the OTC drug review (Docket No. FDA-1976-N-0272 (formerly 76N-0056)); and

Group 3: Combinations containing theophylline, ephedrine, and hydroxyzine HCl (Docket No. FDA-1978-N-0701 (formerly 78N-0070)).

With respect to the products in Group 2, a notice of opportunity for hearing was published on April 9, 1976 (41 FR 15051). No hearing was requested, and approval of applications for products covered by Docket No. FDA-1976-N-0272 (formerly 76N-0056) (DESI 1626) were withdrawn by notice in the Federal Register published October 7, 1977 (42 FR 54620).

With respect to the products in Group 3, FDA granted a hearing in response to requests (49 FR 36443, September 17, 1984). The hearing requests were subsequently withdrawn, and approval of applications for products covered by Docket No. FDA-1078-N-0701 (formerly 78N-

0070) (DESI 1626) were withdrawn by notice in the Federal Register published July 8, 1998 (63 FR 36923).

With respect to the products in Group 1, in 1976, FDA granted temporary permission for the products to remain on the market because similar products had been marketed OTC in the past and were then undergoing review in the Over-the-Counter Drug Study (41 FR 15053, April 9, 1976). In 1984, FDA amended the April 1976 notice to include its analysis of new information regarding combination products containing a xanthine derivative (49 FR 7454, February 29, 1984). Based on its analysis of the new information, FDA concluded that there is a lack of substantial evidence: (1) That each ingredient contributes to the claimed effect of such combination drug products and (2) that the dosage of each component is such that the combinations are safe and effective for a significant patient population (49 FR 7454). Therefore, FDA proposed in the 1984 notice to withdraw approval of the applications for combination products containing a xanthine derivative and offered an opportunity for hearing regarding its proposal.

At the time of the July 24, 2012, notice, there was one outstanding hearing request under Docket No. FDA-1976-N-0344 (formerly 76N-0057) filed by William P. Poythress & Co, Inc., 16 N. 22nd St., P.O. Box 26946, Richmond, VA 23261, regarding an unidentified product containing a xanthine derivative, ephedrine, and 8 mg or less of phenobarbital. FDA was unable to find current contact information for William P. Poythress & Co, Inc. In the July 24, 2012, notice FDA provided this company an opportunity to withdraw or affirm its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

C. Docket No. FDA-1979-N-0224 (Formerly 79N-0169) (DESI 12283)

In 1979, FDA announced its DESI conclusions regarding the effectiveness of chlorthalidone for the treatment of hypertension and certain types of edema (44 FR 54124, September 18, 1979). Specifically, FDA determined that there was substantial evidence to support the effectiveness of the 25- and 50-mg strengths for use in hypertension and edema, but that there was no longer justification for the 100-mg dosage form of chlorthalidone because of safety concerns at that dosage level (44 FR 54124 at 54126). In the 1979 notice, FDA proposed to withdraw approval of the 100-mg strength and offered an opportunity for hearing regarding its proposal.

At the time of the July 24, 2012, notice, there was one outstanding hearing request under this docket filed by Generics International Division of Apotex, Inc., 2400 North Commerce Pkwy., suite 400, Weston, FL 33326, regarding chlorthalidone. In the July 24, 2012, notice, FDA provided this company an opportunity to withdraw or affirm its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

D. Docket No. FDA-1983-N-0297 (Formerly 83N-0030) (DESI 50213)

Under Docket No. FDA-1983-N-0297 (formerly 83N-0030), FDA evaluated the evidence of effectiveness for certain fixed-combination drugs containing antibiotics and sulfonamides and determined that these products lacked substantial evidence of effectiveness (34 FR 6008, April 2, 1969). In the April 1969 Federal Register notice, FDA proposed to revoke provisions for certification of these products, and offered interested persons 30 days to submit data concerning the proposal. Data submitted in response to the April 1969 notice did not provide substantial evidence of effectiveness, so FDA amended the antibiotic regulations on June 30, 1970, by revoking provisions for the certification of these drugs (35 FR 10587, June 30, 1970). The order

was to become effective in 40 days and allowed 30 days for interested persons to file objections and request a hearing. The time for responding to the June 1970 order was subsequently extended until August 17, 1970 (35 FR 12653, August 8, 1970).

In response to the June 1970 order, Pfizer Inc. submitted data regarding its affected product, Urobiotic 250 Capsules, and requested a hearing. Despite the filing of timely objections, the amendments were inadvertently not stayed, and succeeding codifications of the antibiotic regulations did not explicitly provide for certification of Urobiotic 250 Capsules. However, FDA permitted Pfizer to continue distribution of its product pending resolution of the firm's hearing request. In July 2010, Pfizer voluntarily withdrew its application for Urobiotic (see 75 FR 42455, July 21, 2010).

At the time of the July 24, 2012, notice, there was one outstanding hearing request under this docket filed by Pfizer, Inc., 235 East 42nd St., New York, NY 10017, regarding Urobiotic. As noted in the previous paragraph, the product itself was withdrawn, but FDA attempted to contact the company to verify that it no longer wished to pursue its hearing request. The company did not respond, and in the July 24, 2012, notice, FDA provided this company an opportunity to withdraw or affirm its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

II. Resolution of Hearing Requests Pertaining to Dockets Subject to This Notice

The time period for responding to the July 24, 2012, notice has elapsed, and no companies with outstanding hearing requests pertaining to the dockets listed in this document responded to the notice. Because no outstanding hearing requests relating to these dockets were affirmed in response to the July 24, 2012, notice (or in response to FDA's previous attempts to contact companies with outstanding hearing requests), all of the outstanding hearing requests

pertaining to Docket Nos. FDA-1975-N-0355 (formerly 75N-0185) (DESI 3265); FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), and FDA-1978-N-0701 (formerly 78N-0070) (DESI 1626); FDA-1979-N-0224 (formerly 79N-0169) (DESI 12283); and FDA-1983-N-0297 (formerly 83N-0030) (DESI 50213) are deemed to be withdrawn.

Effective as of the date of this notice, it is unlawful to introduce into interstate commerce any of the products identified in any of the dockets included in this notice, or any IRS product to any product identified in these dockets, that is not the subject of an approved NDA or ANDA. Any person who wishes to determine whether a specific product is covered by this notice should write to the Center for Drug Evaluation and Research (see ADDRESSES).

III. Discontinued Products

Some firms may have previously discontinued manufacturing or distributing products covered by this notice without removing them from the listing of their products under section 510(j) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360(j)). Other firms may discontinue manufacturing or distributing listed products in response to this notice. Firms that wish to notify the Agency of product discontinuation should send a letter identifying the discontinued product(s), including the National Drug Code number(s), and stating that the manufacturing and/or distribution of the product(s) has (have) been discontinued. The letter should be sent electronically to Sakineh Walther (see ADDRESSES).

Firms should also electronically update the listing of their products under section 510(j) of the FD&C Act to reflect discontinuation of products covered by this notice. Firms should be aware that, after the effective date of this notice, FDA intends to take enforcement action without further notice against any firm that manufactures or ships in interstate commerce any unapproved product covered by this notice.

Dated: January 6, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2014-00256 Filed 01/09/2014 at 8:45 am; Publication Date: 01/10/2014]